REMARKS

The Office Action mailed 9 April 2003, has been received and its contents carefully noted. The pending claims, claims 32-50, were rejected. Claims 34-48 were withdrawn from consideration. Claims 32, 33, 49, and 50 were rejected. By this amendment, claims 34-48 have been cancelled and claims 51-56 have been added and claims 33 and 49 have been amended. Support may be found in the specification and claims as originally filed. Specific support may be found on page 28, lines 21-22, page 31, lines 9-10, page 38, lines 6-8, and page 43, lines 24-26. No statutory new matter has been added. Reconsideration is respectfully requested.

Restriction Requirement

The Examiner required a second Restriction Requirement. In particular, the Examiner further restricted the claims into four groups as follows:

I. Claims (in part) 32, 33, 49, and 50 drawn to a compound of claim 32.

II. Claims (in part) 32, 33, 49, and 50 drawn to compounds not included in Group I.

III. Claims (in part) 32, 33, 49, and 50 drawn to complex binary compositions and method of antimalarial chemosensitizing.

IV. Claims (in part) 32, 33, 49, and 50 drawn to compositions and method of modulating resistance to antimalarial activity.

Applicants respectfully elect Group I for further prosecution. In a telephone conversation with the Examiner on or about 18 April 2003, the Examiner indicated that the claims of Group I are patentable over the prior art and would be allowable if the rejection under 35 U.S.C. 112, second paragraph, is overcome.

Rejection under 35 U.S.C. 112, second paragraph

Applicants respectfully submit that the remaining issues under 35 U.S.C. 112, second paragraph, are whether the terms "antimalarial" and "administering" are clear and definite.

With regard to the indefiniteness rejection of "antimalarial", Applicants respectfully submit that the specification provides examples of various antimalarials. See, for example, page 28, lines 21-22, page 31, lines 9-10, page 38, lines 6-8, and page 43, lines 24-26.

Additionally, Applicants again respectfully submit that the term "antimalarial" is not indefinite as it is a term commonly used by those skilled in the art to refer to various compounds known in the art that exhibit activity against *Plasmodium spp.* For example, see the various references provided with the Invention Disclosure Statements submitted by Applicants.

- Schmidt, "Plasmodium Falciparum and Plasmodium Vivax Infections In The Owl Monkey (Aotus Trivirgatus)", Am. J. Trop. Med. Hyg., Vol. 27(4): pgs. 703-717, (1978).
- Milhous et al., "In Vitro Strategies for Circumventing Antimalarial Drug Resistance", Antimicrobial Agents Chemother, (1985),Vol. 27: pgs. 525-530,.
- Oduola et al., "Reversal of Mefloquine Resistance with Penfluridol in Isolates of Plasmodium Falciparum from South-West Nigeria", (1993), Transactions of the Royal Society of Tropical Medicine and Hygene, 87:81-83.
- Chulay et al., "Plasmodium Falciparum: Assessment of in Vitro Growth by [^{3}H] Hypoxanthine Incorporation", (1983), Experimental Parasitology, 55:138-146.
- Gerena, L., et al., "Fluxetine Hydrochloride Enhances In Vitro Susceptibility To Chloroquine In Resistant Plasmodium Falciparum", (1992) Antimicrobial Agents and Chemotherapy 36:2761-2765.
- Kyle, D.E., et al., "Plasmodium Falciparum: Modulation By Calcium Antagonist Of Resistance To Chloroqine, Desethylchloroquine, Quinine, and Quinidine In Vitro", (1990) In Vitro. Trans Royal Soc. Trop. Med. Hyg. 84:474-478.
- Desjardins, R.E., et al., "Quantitative Assessment of Antimalarial Activity In Vitro by a Semiautomated Mdilution Technique", (1979) Antimicrobial Agents Chemother 16:710-718.
- Foote, *et al.* "The Mode of Action and the Mechanism of Resistance to Antimalarial Drugs" (1994) Acta Tropica 56:157-171.

A few examples of antimalarials recited in the references cited above include: chloroquine, quinine, mefloquine, amodiaquin, primaquine, pyrimethamine, sulfonamides, sulfones, dihydrofolate reductase inhibitors, tetrandine, and derivatives thereof. It is important to note that those skilled in the art commonly use the term "antimalarial" to refer to compounds that show activity against *Plasmodium falciparum* and P. *vivax* which is also evidenced in the references cited above.

Further, there are numerous assays for determining whether a given compound has activity against malaria, e.g. prevent or inhibit parasitic growth, that are known in the art. See, for example, the specification, Chulay *et al.* (cited above), Desjardins *et al.* (cited above), and etc. The eBook entitled Malaria Methods and Protocols (2002) ISBN: 1-59259-271-6, by Doolan, Denise L. (Naval Medical Research Center, Silver Spring, MD) provides many different

protocols for determining whether a compound is an "antimalarial". Clearly, one may readily determine whether a given compound is an "antimalarial" according to the present invention.

Moreover, the following Internet sites - http://www.hendrickhealth.org/healthy/000116.htm and http://www.chclibrary.org/micromed/00037960.html state "Antimalarial drugs are medicines that prevent or treat malaria" as a definition for "antimalarials".

Two on-line medical dictionaries define "antimalarial" as "1. Preventing or curing malaria. 2. A chemotherapeutic agent that inhibits or destroys malarial parasites. (05 Mar 2000)" See http://www.medical-dictionary.com/results.php and http://cancerweb.ncl.ac.uk/cgi-bin/omd?query=antimalarial&action=Search+OMD.

The on-line Miller-Keane Medical Dictionary, 2000, defines "antimalarial" as "(an´´tî-mah-lar´e-al) 1. therapeutically effective against malaria. 2. an agent that is therapeutically effective against malaria." See http://my.webmd.com/content/miller_keane/7/miller_keane_3048.htm?lastselectedguid={5FE84E90-BC77-4056-A91C-9531713CA348}

The Medterms.com Medical Dictionary defines "antimalarial" as "a drug directed against malaria". See http://www.medterms.com/Script/Main/art.asp?li=MNI&ArticleKey=16900.

The eBook entitled Antimalarial Chemotherapy Mechanisms of Action, Resistance, and New Directions in Drug Discovery (2001) ISBN: 1-59259-111-6, by Rosenthal, Philip J. (University of California at San Francisco, CA) provides many different antimalarials and their mechanisms of action.

Clearly, all the above citations evidence that one skilled in the art understands the scope and meaning of "antimalarial". Therefore, Applicants respectfully submit that the meaning of the term "antimalarial" is not indefinite. Therefore, the rejection under 35 U.S.C. 112, second paragraph, should properly be withdrawn.

Applicants also respectfully submit that the term "administering" is clear and definite. Specifically, one skilled in the art understands the scope and meaning of a method step which recites "administering" a compound or drug to a subject. In fact, the United States Patent and Trademark Offices grants claims comprising steps wherein nothing more than the term "administering" is required for clarification. See, for example, the following patent claims that

have been issued by the present Examiner wherein nothing more than the step of "administering" a given compound was required for the treatment claims:

1. U.S. Patent No. 6,555,542 Assistant Examiner: Patel; Sudhaker B.
"12. A method for treating Factor Xa-associated disorders selected from thromboses, coronary artery disease or cerebrovascular disease, which comprises ***administering*** to a mammalian species in need thereof a therapeutically effective amount of at least one compound of claim 1."

2. U.S. Patent No. 6,552,025 Assistant Examiner: Patel; Sudhaker B.
". A method of inhibiting sphingolipid metabolism associated with a cell signaling pathway disease or disorder, comprising ***administering*** to a patient having the disease or disorder, a therapeutic dose of a composition comprising a diimino compound in a cationic form; wherein the diimino compound has a molecular weight between 112 and 3000 Daltons; and wherein the diimino compound has the following structural formula: ..."

3. U.S. Patent No. 6,548,547 Assistant Examiner: Patel; Sudhaker B.
"2. A method for activating soluble guanylate cyclase, which comprises ***administering*** to a host in need of the activation at least one compound as claimed in claim 1."

4. U.S. Patent No. 6,548,514 Assistant Examiner: Patel; Sudhaker B.
"16. A method of treating a disease or medical condition mediated by the production or effect of cytokines, which method comprises ***administering*** to a warm-blooded animal in need thereof a cytokine inhibiting amount of a compound of the Formula I, or a pharmaceutically-acceptable salt or in-vivo-cleavable ester thereof, according to claim 1."

5. U.S. Patent No. 6,548,505 Assistant Examiner: Patel; Sudhaker B.
"4. A method of cancer radiotherapy which comprises ***administering*** to a subject in need of such therapy an amount effective to protect biological material of the subject from

ionizing radiation damage of a compound of formula (I) effective to minimise damage to non-tumour cells and tissues, and subjecting the locus of a tumour in the subject to an ionizing radiation source: ..."

6. U.S. Patent No. 6,548,504 Assistant Examiner: Patel; Sudhaker B.
"10. A method of treating Alzheimer's disease, schizophrenia or depression comprising ***administering*** to a patient in need of treatment a safe and therapeutically effective amount of a compound according to claim 1."

If necessary, Applicants will provide many more examples of such method claims that only recite "administering" a given compound that have been allowed by the present Examiner and other examiners.

Additionally, Applicants respectfully submit that the specification provides numerous examples of how the claimed compound may be administered, e.g. orally, rectally, transdermally, subcutaneously, intravenously, intramuscularly, intranasally, and ocularly. See Specification, pages 45-51. Therefore, Applicants submit that the step and term "administering" in the claims is clear and definite and that no clarification is required.

Since the scope and meaning of "administering" is clear and definite, the rejection under 35 U.S.C. 112, second paragraph, should properly be withdrawn.

Request for Interview

Applicants respectfully request either a telephonic or an in-person interview should there be any remaining issues.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. **210-380**, referencing Attorney Docket No. **P66823US0 (01-06).**

Respectfully submitted,
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